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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/127,138	07/31/1998	MICHEAL L. GRUENBERG	24731-500E	9760

25225 7590 02/23/2004  
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EXAMINER

SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 02/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/127,138	GRUENBERG, MICHEAL L.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Ron Schwadron, Ph.D.	1644	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

3/20/2003  
11/24/2003  
6/20/2003

- 1) ☒ Responsive to communication(s) filed on 6/20/2003.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 154-160 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 154-160 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                                    |

1. Applicant's election without traverse of the species anti-IL-4 antibody in the Paper filed 6/20/2003 is acknowledged.
2. Claims 154-160 are under consideration.

### RESPONSE TO APPLICANTS ARGUMENTS

3. Regarding priority to parent application 60/044693 for the purposes of prior art, there is no disclosure in parent application 60/044693 of the method of claim 157 which recites all of the particular antibodies and combinations recited in said claim. Therefore, said claim is not entitled to priority to application 60/044693 for the purposes of prior art.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 154-160 are rejected under 35 U.S.C. 103(a) as being unpatentable over June et al. (US Patent 6,352,694) in view of Hsieh et al. and Cracauer et al.

June et al. teach that Th1 cells can be produced and expanded using treatment of CD4+ T cells with antiCD3 antibody and antiCD28 antibody (see column 30, penultimate paragraph). Said method does not use exogenous IL-2. June et al. teach that the CD4+ cells used can be antigen specific (see column 30, first complete paragraph). The antiCD3 and antiCD28 antibodies taught by June et al. are mitogenic monoclonal antibodies (see Example 14). The cells can be further isolated or purified

(see column 19). The starting material can be human T cells isolated from PBL (see column 19). The cells can be expanded to reach greater than  $10^{10}$  cells (see column 28, lines 1-5 and column 54 ). The cells are administered in vivo to the individual from which they were derived (eg. autologous cell therapy, see columns 27-30). The cells are homogenous because June et al. teach that this method selectively expands Th1 cells (see column 30, penultimate paragraph). The antiCD3 and antiCD28 antibodies can be monoclonal antibodies (see column 5, last paragraph and column 7, first paragraph). June et al. do not teach that the cells are grown at the specific concentration recited in claim 154 or the addition of anti IL-4 antibody. Cracauer et al. teach hollow fiber bioreactors and the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro (see columns 1-3) wherein concentrations of greater than  $10^8$  cells per ml are achieved (see column 5, last paragraph). Hsieh et al. teach that neutralizing IL-4 with antiIL-4 mab resulted in production of Th1 cells (see page 6066, second column). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because June et al. teach that Th1 cells can be produced and expanded using treatment of CD4+ T cells with antiCD3 antibody and antiCD28 antibody wherein said method does not use exogenous IL-2 whilst Cracauer et al. teach hollow fiber bioreactors and the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro wherein concentrations of greater than  $10^8$  cells per ml are achieved and Hsieh et al. teach that the addition of antiIL-4 antibody to T cells in vitro favors the development of Th1 cells. One of ordinary skill in the art would have been motivated to do the aforementioned because Cracauer et al. teach hollow fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro (see columns 1-3). One of ordinary skill in the art would have been motivated to do the aforementioned because Hsieh et al. teach that IL-4 increases Th2 in a concentration dependent fashion (see Table 2) and therefore addition of antiIL-4 at the appropriate concentration could be used to effectively prevent virtually any Th2 cells from being produced.

6. No claim is allowed.

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached Monday to Thursday from 7:00am to 6:00pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit: 1644



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PRIMARY EXAMINER  
GROUP 1800 1644

Ron Schwadron, Ph.D.

Primary Examiner

Art Unit 1644